Da Costa, (J. M.) & Longstreth. (M)

With kind regards,

M. L.

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RESEARCHES ON THE STATE OF THE GANGLIONIC CENTRES IN BRIGHT'S DISEASE.

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These researches were begun in the spirit of pure investigation, since, so far as we were aware, no observations had been made of the condition of the ganglia or nerves supplying the kidneys in Bright's disease —a disease in which, as all are agreed, great alterations in the vessels and in the vascular supply, not only of the urinary secreting organs, but of the whole body, exist, or are brought about as the results of secondary changes. It seemed to us, therefore, that some morbid condition ought to be met with in the nervous arrangements that have for their chief office the regulation of the blood supply. Moreover, reflecting on the fact that the kidney affection is always both sided, and on the nervous phenomena which so often attend Bright's disease, we thought that exploration of the nervous system, especially of the ganglionic nervous system, might throw some light alike on the origin of the complaint and the accompanying signs of nervous disturbance. But while we were of the opinion that some altered states would be found to exist in the nervous centres, of the nature of such alterations we had no theory and no conclusions to substantiate; and now for the first time, more than a year subsequent to the investigation of the last case given in this series, and more than four years since our first observations, we attempt to formulate the results of the work. In the mean time, many cases of Bright's disease, in one or other of its many forms, have been partially investigated, but are not included in the present series, because we feared that they would vitiate the results, as some were cases of amyloid degeneration, others were complicated with coexist-

ing chronic disease of different character, and as in others, again, the specimens were not treated in precisely the same manner as was done with all the specimens in the present series.

In the first investigations, the nerve-trunks supplying the kidney were examined, but the results furnished nothing satisfactory. In all the present published cases, the method of treating the specimens—we refer particularly to the ganglia—was invariably the same; so that whatever criticism is made of the conclusions arrived at, none of the ante-mortem conditions, so far as preserved at the time of the autopsy, have been varied by irregularities of preparation. The difficulties of obtaining the ganglia were great, and the specimens required a long dissection, which was performed while they were kept submerged in the preservative fluid. The separation and isolation of the ganglia were rendered difficult by large amounts of fat surrounding them, inclosed in a firm connective tissue; the exceptions to this condition were found in Cases 7, 8, and 9, and partially in Case 6. The ganglia were obtained by removing, along with the kidneys and suprarenal capsules, all the structures in front of the vertebral column, including the aorta and cœliac axis, the attachments of the diaphragm, and the splanchnic nerves. From this mass the connective and adipose tissues were carefully separated, leaving the solar plexus and its nerve-branches. The portion of the ganglia examined microscopically was that from which the nervous filaments were given off for distribution to the kidney; other portions of the ganglia were also examined for comparison.

Let us now take a set of cases in which striking pathological changes were discovered.

Case I.—This was a case of a single lady, aged 43, seen by one of us in connection with an eminent physician of Philadelphia. She had been at times under his care for a year with dyspeptic symptoms, but otherwise appeared in fair health; there was not a particle of dropsy. Spending the summer at the sea-shore, she had not been under observation immediately before the fatal illness, and sent for her physician in consequence of nausea and vomiting and some shortness of breath. A marked pericardial friction sound was detected, and an examination of the urine showed it to contain about one-third of the test-tube full of albumen and granular tube-casts. The malady became now as markedly vehement as previously it had been latent; twitching of the muscles, followed by general convulsions, set in. These were succeeded by uræmic coma, and death took place in about a week after the development of the pericarditis.

Post-mortem Examination, by Dr. Longstreth. November, 1877.—*Cavities.*—There was considerable serum in the peritoneal cavity, but no lymph. The *pleural* cavities contained more than the usual serum, which was bloodstained; but no lymph. The surface of the pleura was injected. There were some old adhesions on both sides. The *pericardium* showed an intense pericarditis. The walls were thickened, the sac distended with clouded serum and a large amount of lymph. The lymph lay in folds, was recent, and could be torn off from the surface of the heart or of the sac, leaving the membrane rough and displaying injected vessels.

Heart.—The ventricles were uncontracted, and contained a small

amount of blood and recent clots, less on the left side than on the right. The organ was of small size; its left ventricle hypertrophied. The cavities, orifices, and valves normal; the muscular structure firm and of dark colour, especially near the surface. The other organs of the body presented nothing of note, except the urinary apparatus.

The *kidneys* were much reduced in size, pretty regular in outline, but with a nodulated surface. The veins showed prominently on the surface of the capsule. The cortex was greatly wasted, in most parts barely forming a covering at the bases of the pyramids. The interpyramidal portions were reduced to a lesser degree, but had also suffered contraction. The straight tubes of the pyramids were twisted near the base. The colour of the pyramids was redder than the cortex, which presented an opaque striated appearance. The capsule was much thickened, and tightly adherent. After removal the surface of the kidney was found highly granular and nodular. The capsule did not tear the kidney on removal because of the great firmness of the organ, which was dense like cicatricial tissue. The kidney had a highly urinous odour, and was imbedded in a thick layer of fat, although the adipose tissue at other parts of the body was reduced in amount.

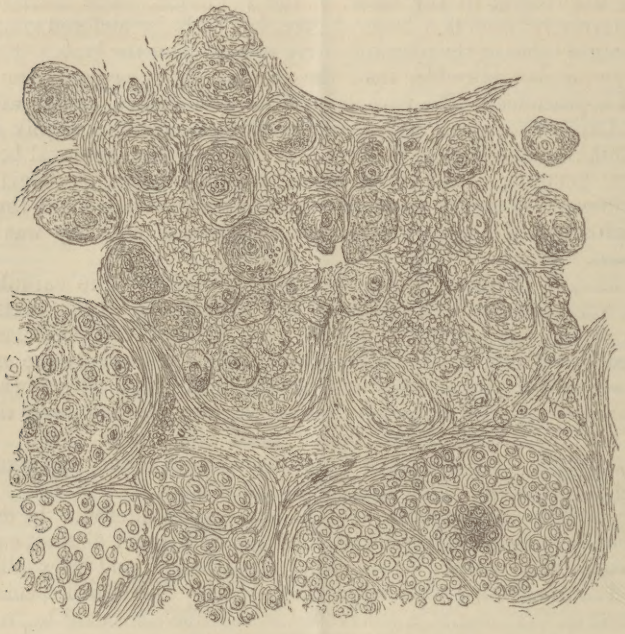
Microscopic Examination of the Renal Ganglia.—The capsule of the ganglia was composed of a broad band of thick-fibred closely-matted connective tissue; no cellular elements were present. Its vascular supply consisted of numerous large thick-walled vessels, especially the muscular tunic; scarcely any capillaries were visible in it. The adipose tissue was in large amount. The connective tissue was very marked along the nerve trunks, and penetrated the ganglion mass along with them. At the peripheral portion it encroached upon the nervous tissue, and sent into it bands of coarse fibres which will be described later.

The ganglion cells were in the highest degree altered. In unstained specimens they mostly appeared as yellow spots without distinct structure; rarely could any nucleus or nucleolus be detected, and very often they appeared as areas filled with large oil-globules. In stained specimens, in some parts of the ganglia, a shrivelled small nucleus could be frequently discerned, and more frequently the nucleolus; at other parts the condition of the cells was no better than that already referred to in the unstained specimen—the cell body filled with granules and fat, often considerable pigment, the nucleus and nucleolus nearly or quite invisible. Many of the cells were reduced in size, especially those showing markedly degenerated conditions; their outlines were irregular and sometimes puckered or folded. In many parts of the ganglia the whole substance over small areas was converted into a granular and fatty mass, the ganglion cells as well as the surrounding connective tissue having degenerated.

The connective substance of the ganglia everywhere presented a coarse, closely-matted, firm, fibrous appearance. It was generally devoid of cells, or, where these elements were present, they were highly granular and fatty. The cells were rounded in form; no elongated or spindle-shaped bodies were visible. This connective tissue encroached closely upon the ganglion cells, and often formed concentric coarse-fibred rings around them. The connective tissue entered the ganglionic mass along with the nerve trunks, and penetrated it from the envelope. It passed through the interior as broad bands of fibrillated tissue, which partitioned off the ganglion cells into very distinctly-formed compartments, often containing but a single cell, or twos and threes. The cells around which the con-

nective substance was the firmest generally showed greater degenerative changes than their fellows, but this appearance did not universally hold. The connective tissue development was often most marked in the central portions of the ganglia; it was by no means the condition universally found at the peripheral portions in connection with the thickening of the capsules.

Fig. 1.



At the left of the figure are seen the nerve-tubules in cross section, surrounded with increased connective tissue continuous with that covering the ganglia. The ganglionic cells show numerous oil-globules and granules. The basis substance between the cells is fibrous in character, and granular and fatty changes are present. × 350.

The vessels of the ganglia were not numerous; they were of large size, with thickened walls, and surrounded by large amounts of firm connective tissue, in which lymphatic vessels were visible. This case, indeed, was the only one in which the lymphatic vessels were discovered within the ganglionic mass, although vessels of this character were seen not unfrequently in the connective capsules in the other cases. The vessels were generally found empty, and some had collapsed from the contraction of the connective-tissue growth around them. In a few instances evidences of old hemorrhages in the interior of the ganglia, near some of its vascular trunks, were encountered, but none of them were of recent date.

The microscopic changes in the ganglia in this case were then of striking character, and involved all the component parts. The connective tissue covering the nervous mass was very much thickened; the con-

nective substance in the interior presented a firm fibrous appearance. The ganglion cells showed advanced degenerative changes, and were in many parts barely recognizable. The vascular supply exhibited marked alterations from the normal condition; thickening of the vessel walls, hypertrophy of the muscular coat, and increase of the surrounding connective tissue, with collapse and closure of their lumina.

The post-mortem examination proved that the kidney disease was of long standing, and that the contraction of the organ had advanced very far. A careful microscopic study showed the changes to be similar to those usually found in kidneys presenting the gross appearances already described.

Case II.—Mary A. D., æt. 60, widow, was admitted to the Pennsylvania Hospital, December 24, 1878. She was picked up in the street in an unconscious condition and brought to the hospital at 9.15 P.M. No history could be obtained as to her previous health. She could be only very slightly aroused, but did not speak. The pulse was 90 per minute, strong and full; respiration 28, and rather laboured. The right pupil was contracted to about one-third below the average size, and the left one as markedly dilated; both were insensible to light. Over the whole chest loud mucous râles were heard, so loud that the character of the heart-sounds could not be determined. There was no obvious paralysis. Her breathing gradually became stertorous, and slight convulsive movements of the muscles were noticed every few minutes, lasting a few seconds. There was no œdema of any part of the body. Her urine, drawn with catheter, was found to contain a large amount of albumen (about one-third), and the microscope showed the presence of granular casts. The patient died eight hours after admission.

The *post-mortem examination* was made by the Coroner's physician, and no accurate notes were obtained. A large apoplectic clot was found in the left half of the brain. The kidneys were very considerably contracted, and many small cysts were present on their surface. The capsule was thickened and adherent, and the cortex was very greatly reduced in thickness. The organs were imbedded in a large amount of fat, and had a strongly urinous odour.

The surface of the *kidney*, as seen in the microscopic section, was highly granular; the capsule was thickened, and was composed of coarse-fibred connective tissue, closely matted together. Numerous large and small sized vessels were distributed through it, and in places they connected with the vascular supply of the cortex. The lymph spaces in the capsule were not numerous or large. The union to the cortical tissue was very intimate, and in many places the capsule dipped down and was continuous with broad connective-tissue bands in the periphery of the organ. The point of junction between the two was marked by the aggregation of round cells, which stained very deeply with carmine. Several cysts were seen on the surface, mostly occupying the cortical tissue, but also projecting and causing a prominence of the capsule.

The thickness of the cortex was greatly reduced; under a magnifying power of 50 diam. its width occupied a little more than the breadth of one field of the microscope. The arrangement of the component parts in the cortex was found much altered; the Malpighian bodies were very irregularly placed, and the tubes of the cortical pyramids pursued a twisting

direction. The Malpighian bodies were of pretty regular outline, but were surrounded by a broad capsule of connective tissue, which presented a swollen appearance, and contained many new cellular elements, mostly spindle shaped. The Malpighian bodies frequently appeared as homogenous, concentrically arranged connective-tissue masses, without cellular elements and without traces of the capillary tufts. In other parts the capillary tufts were indistinct from the presence of cellular collections themselves granular and indistinct, but in some they were injected and the blood corpuscles were readily distinguishable. The convoluted tubes were irregular in outline, their basement membranes moderately swollen; their epithelial cells were very granular and a little fatty; their nuclei generally obscured and staining poorly with carmine. In other tubes the nuclei were sharply defined and well coloured, but the bodies of the cells were still very granular, but less so than in the other instances. Many tubules were filled with casts or granular matter.

The connective tissue between the tubules was everywhere swollen and increased; in many parts of the cortex it was packed full of cellular elements, both round and spindle-shaped; so great were these collections of cells that in places the outlines of the tubules were concealed; in other parts the tubular structure was lost in firm, coarse-fibred connective tissue. The various parts of the cortex exhibited great differences in the degree of alteration which had taken place in it.

The branches of the renal artery at the bases of the pyramids showed as widely stretched-open, thickened walled vessels, surrounded by an increased amount of connective tissue. The muscular coat was greatly hypertrophied. The connective tissue around the vessel was prolonged into the cortex, and in places was filled with cells which obscured the tubules, but in other places there was a coarse-fibred overgrowth which had destroyed the cortical structure and into which small hemorrhages had taken place.

The vessels of the cortex showed greatly thickened walls, but their course was so altered from the straight direction that they could not be traced. The straight tubes of the medullary cones showed no changes, but the vasæ rectæ were dilated and injected, and the connective tissue around them was increased.

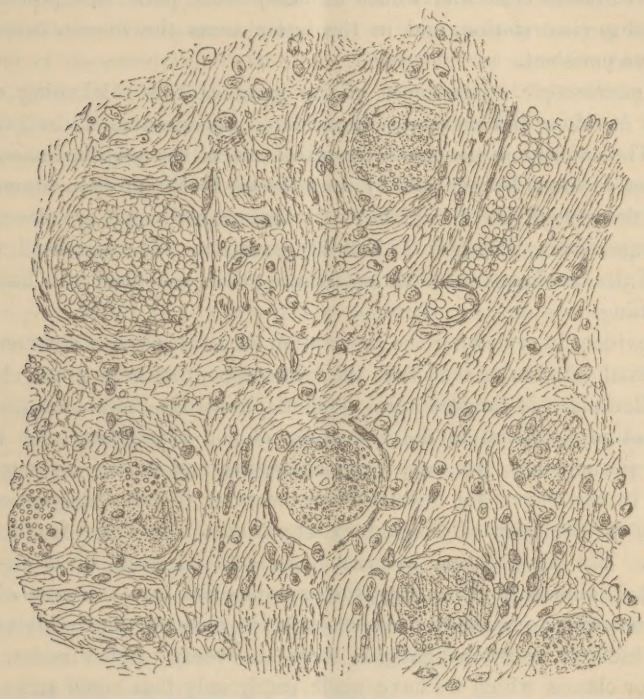
The *ganglionic masses* were enveloped by a thick layer of connective tissue, richly supplied with bloodvessels and encroaching on the nervous tissue and also accompanying the nerve trunks at their exit from the ganglia. There was a considerable mass of adipose tissue around this tissue. The nerve trunks showed an increased amount of connective tissue in their interior as well as surrounding them, but neither here nor in the connective tissue enveloping the ganglia was there any abnormal abundance of cellular elements.

The ganglionic cells were much altered. They appeared shrunken, and their outline was indistinct. The nuclei and nucleoli were difficult to make out. The cell bodies were more or less filled with fatty granules, in some cases occupying nearly its whole space, in others collected in heaps, or else isolated and scattered through the interior. They were also generally markedly pigmented.

The tissue of the ganglia was composed of finely striated connective tissue, in most places clear and nearly transparent, or else having a granular aspect; in other parts, generally towards the periphery, there were present in it pale, usually indistinct, and poorly stained round cells or

nuclei. In the peripheral portions the ganglionic cells, when not overlaid and obscured by the new cellular elements, generally showed their structure more distinctly than in the parts more central.

Fig. 2.



The ganglionic cells show fatty degeneration, and their outlines are indistinct; their nuclei and nucleoli obscured. The basis substance is fibrous and contains some cellular elements. The vessels are large and filled with blood-corpuscles. × 350.

Many large capillary vessels were seen, especially near the superficial portions of the ganglia, entering it either from the connective tissue or along the nervous trunks; in the interior the vessels were of smaller lumen and surrounded by especially thick connective tissue.

The general aspect of the sections in this case gave the impression of degeneration of the ganglionic cells of marked degree, and of a connective-tissue overgrowth within the ganglia which had progressed beyond the stage of granulation tissue to completely formed fibres in which the cellular elements were no longer visible.

We shall not dwell on the interesting clinical questions here connected with the profound coma, the state of the pupils, and the double lesion which determined the symptoms, but, in accordance with our purpose, pass on to an examination of the renal affection.

The appearances of the kidneys and their microscopic examination show conclusively that the renal disease was of long duration, and was of

that form which is so frequently unattended with the obvious symptoms of Bright's disease. The contraction of the organ is found not to be equally complete at all parts. In many the process of interstitial inflammation is still in progress, evidenced by the presence of the numerous connective-tissue elements, whilst in many other parts this process has advanced to cicatrization, and in the latter areas the vessels, tubes, and cells have perished.

The microscopic appearances of the ganglia show thickening of the capsular envelope and markedly degenerated appearances of the ganglion cells. The changes in the connective substance of the ganglia demonstrate a connective-tissue hyperplasia by the increased cellular elements and increased firmness of the fibres; but both these constituents are also undergoing degenerative changes, for both are granular. The increased vascularity of the specimens is a striking feature; their vascularity is, however, diminishing.

It is evident in reviewing the description we have given of the condition of the renal ganglia, as seen with the microscope, that very grave changes have taken place in the structural elements, and that these changes were somewhat proportional to the alterations of the kidney and also to the clinical phenomena. In fact, while arranging and classifying our cases for use in this paper, the question arose whether the classification should be made on the basis of the kidney alterations or on those found in the ganglia. But this question in great degree solved itself, for it was soon found that, viewed in either way, the examples fell into the same classes. We do not wish to imply that the cases, in the changes they exhibit either of the kidneys or in the ganglia, form an evenly graded series. The groups or classes which we have made imply only that some cases show greater changes than others, and not that the changes of one class are of different character from those found in the other; the classification, in other words, is made on the basis of quantity rather than of quality.

In group I. are then the cases with the most striking alterations. The first is a well-marked one of chronic Bright's disease with contracted kidney, characterized by a long period of latency of the symptoms, followed by an outburst of inflammation of the serous membranes, which acted as the proximate cause of death. In the second case, the ante-mortem conclusion that the kidneys were much diseased was confirmed by the autopsy, and the death here resulted, as so frequently occurs in cases of contracting kidney, from cerebral hemorrhage. The kidneys in each of these instances belong to the variety characterized by the results of interstitial inflammation, and the changes in the muscular coats of the arteries were such as are usually found in this variety.

Without further particularizing the kidney changes, let us see what are the alterations in the ganglia, and what conclusions are to be drawn from the microscopic appearances presented. In the first place we wish to

emphasize the condition of the tissues surrounding not only the kidney but the ganglia, viz., the accumulation of fat around the former, and the firmness and tight adherence of the connective tissue, inclosing in its meshes adipose cells, around the latter. The increase of fat around the kidney in chronic Bright's disease is a condition with which we have long been familiar. The accumulation of fat is invariably very great, irrespective of the condition of the other portions of the body in this respect. In a cadaver in which fat is to a great degree absent from the places in which this tissue usually accumulates, it is nevertheless found in large amount around the contracted kidney. One or even two inches of fat is no unusual amount to be found around these organs even in emaciated subjects dying of chronic contracted kidney. The fat, too, is firmly adherent to the organ, and penetrates the chinks around its pelvis, and on the principal section of the kidney is seen to be intercalated with the calyces. The deposit of fat is a very striking condition, and to which hitherto no allusion has been made.

The ganglion cells present changes such as are usually described as fatty degeneration and atrophy. There is breaking down of their substance into granules and fatty globules, which more or less obscure the nucleus, and even when the nuclei are visible they show more or less the same changes.

The connective basis-substance of the ganglia has apparently passed through the active stage of hyperplasia, and is undergoing the contractile process which we are so familiar with in the kidney, and which we have also found to have taken place in the tissues outside the ganglionic masses. This substance has passed the active stage of formation, and its elements also are undergoing degenerative changes.

We shall next look at a series of cases forming a *second group* in which the disease was somewhat different, and the renal changes less marked, though still very obvious.

Case III.—Catherine R., æt. 35, was admitted to the Pennsylvania Hospital, March 24, 1879, suffering from a lacerated wound of the left forearm, caused by falling through a window nine days previously, while drunk. The wound was dressed, and she was attended to daily at the out-patient department until the 24th inst., when she was sent into the wards suffering from severe diarrhœa and incontinence of urine. The patient had been a hard drinker for a long time, and had led an exposed life. The wound was very slow in healing. The urine was albuminous, but, owing to the difficulty in collecting more than a very small amount, no casts were discovered by the microscopic examination. She died suddenly six days after admission, March 30th.

Post-mortem examination, by Dr. Longstreth.—*Cavities.*—The *peritoneum* showed nothing of note. There were many old *pleural* adhesions. The *pericardium* was normal.

Heart.—The ventricles were relaxed. The aortic valves showed old endocardial disease, but were not incompetent. The left ventricle was

slightly hypertrophied, its tissue was pale and less resistant than normal. The cavities were of normal size. Weight, 10 ozs. The *aorta* was dilated, and presented atheromatous changes at its transverse portion. *Lungs.* Both apices showed old cicatricial depressions, and small quiescent cheesy nodules. The *spleen* exhibited a patch of chronic capsulitis, and its fibrous tissue was increased. Weight, 8 ozs. The *liver* was irregular in outline, firm, and reduced about one-half in size. The fibrous tissue was much increased, and its capsules thickened and adherent, leaving on removal a granular surface.

The *kidneys* were reduced in size, presenting a slightly swollen appearance; firm, and irregular in outline. On section, the cortex was found much diminished in thickness, the capsule was tightly adherent and thickened, and on removal left the surface of the organ markedly granular. The urinous odour was very decided. There was no disease of the ureters or bladder. In a microscopic section of the organ, cut vertically, the capsule was seen to be much thickened; it was composed of coarse connective tissue fibres, rather widely separated, and presenting a swollen aspect. The capsular connective tissue was thoroughly permeated by blood and lymph spaces, which gave it a net-like appearance, and its tissue was in places crowded with cellular elements. On the surface of the cortex, in one of the sections, could be seen a small cyst, which had raised the capsule. Both in the capsule and in the cortex at its outer portions the accumulation of cellular elements was especially marked.

The walls of the larger branches of the renal artery, at the junction of the cortex and medullary portions, showed an increase in the thickness of their coats of marked degree; the change was especially noted in the muscular coat; the connective tissue around the vessels was greatly thickened, and in many places was crowded with new cellular elements. The vessels of the cortex (arteriolæ ascendentes) showed dilatation, thickening of their walls, and were tortuous in their course. The thickening consisted in hypertrophy of the muscular cells, the nuclei of the muscular fibres being very distinct. This condition was present in all the arterial vessels, both the larger and the smaller ones.

The condition and appearance of the Malpighian bodies differed greatly in the various parts of the section. Some of the bodies showed but slight increase of their connective-tissue capsules, or whilst in some this connective tissue was swollen and hyaline-looking, its individual fibres were not dense and broadened. In the majority of the bodies the capsules were thickened to three or four times their normal width; in all of them the cellular elements were very abundant, in some crowding the spaces between the capillary loops and even obscuring the vessels. The capillary tufts varied greatly in their condition in different parts of the kidney; in some bodies the circulation was evidently very free, the capillaries having their ordinary calibre; in others, the accumulation of cellular elements was so abundant, and the increase of connective tissue so marked, that the lumina of the vessels were encroached upon. This, at least, was the post-mortem picture presented, whatever may have been the actual state of the circulation during life.

The connective tissue between the convoluted tubules was also increased, varying, however, in different parts of the kidney, from a simple swelling of this tissue, with a greater or less abundance of infiltrated cells, to a heavy-fibred tissue, which was generally devoid of the cellular elements, except in parts near the larger vessels, or near markedly com-

pressed Malpighian bodies. The increase of connective tissue had, of course, led to compression of the tubes; this change was more noticeable at the peripheral portions of the cortex.

The condition of the epithelial cells of the convoluted tubes was in places nearly normal, and in these parts little change was found also in the intertubular spaces; in other parts, the cells were very highly granular, their nuclei obscured, and, in some, fatty changes were evident. A large number of the tubes were filled with tube casts, containing abundance of granular matter and detached and degenerating epithelium.

The straight tubes of the cortical pyramids and the tubes of the medullary cones, as well as their surroundings, showed little change. In the latter set of tubes, a number of tube-casts were visible *in transitu*.

The vascular connection between the cortex and the capsule of the organ was greatly increased, and in many sections large vessels were seen passing both from one to the other, filled with recent coagula, in which the red corpuscles could be discovered. Around these new vascular trunks the cellular infiltration of the tissue was always more abundant, and the intertubular connective-tissue changes most advanced.

Microscopic Examination of the Renal Ganglia.—The periphery of the nervous mass was seen to be surrounded by a broad layer of connective tissue, the individual fibres of which were stout and generally closely matted; in many parts the connective tissue was looser and the meshes filled with adipose cells. The nerve trunks entering the ganglia were also surrounded by a firm connective tissue, more abundant than in the normal condition, which was in parts filled with small cells or nuclei, which very readily took the carmine staining. The fibres of the nerve trunks and also the nerve bands or tracts within the ganglia were normal.

The nerve cells (ganglionic cells) at all parts, though varying in degree in different situations, presented strikingly abnormal conditions. The nucleoli were not visible in the great majority of the cells; in fact, in only a few instances could the nucleoli be seen as clear shining bodies within the nuclei; in others the existence of them could be made out only by the lighter shade of colour at some part of the nuclear body. In no instance did they present a normal appearance. The nuclei stained with carmine but poorly, their outline was often irregular, in some instances angular, and their structure could not be distinctly studied owing to changes in the cell body, but no alteration was found in them.

The bodies of the ganglion cells, in the great majority of cases, were irregularly shaped and angular in outline; some, however, were round and plump looking, and these cells showed their nuclei and nucleoli quite distinctly and in their general appearance were more normal looking. In the majority the cell body was highly granular, and exhibited numerous minute oil globules. The oil globules were irregularly aggregated, in some, occupying a small area at one end of the cell, in others, placed more centrally, close up to the nucleus, and in others, nearly the whole cell body was occupied by them. The degree of fatty change seemed to bear some relation to the shape of the cell, the greater the degenerative changes the more irregular the shape. The processes of the ganglion cells could in many cases be traced a short distance from the cell body.

The substance of the ganglia, the tissue around the ganglionic cells, showed in this case very marked alterations and deviations from the normal. It was made up of an almost transparent granular basis, in which at places a fine striation could be detected. In the basis substance were cells of vary-

ing shape and size, some apparently simple nuclei, others having a very small body containing a relatively large nucleus—the nuclei in both cases were about the same size; others were of irregular shapes, some elongated at one pole, others bipolar, and others presented an elongated spindle-shaped figure, having a centrally placed nucleus and long waving processes. These cells stained deeply with carmine, the nucleus of course taking a deeper coloration, but the whole body of the cell was also more or less coloured, except in some of the more elongated spindle cells, whose processes remained uncoloured. The arrangement of these cells presented no definite regularity. In some places they were heaped up around the ganglion cells, and were frequently seen overlying the cell bodies; in other parts they were less abundant, and often formed a ring or cleared space around the nerve-cells. The spindle-cell processes did not take any general direction, and were often seen lying across each other. The ganglion cells around which were cleared spaces, were usually more normal in appearance than those around which the cells were closely heaped, but exceptions to this rule were noticed.

The vascular supply of the ganglionic tissue was greatly increased; numerous capillaries were found, and numbers of large dilated thin-walled vessels in which the red corpuscles were crowded. The cellular elements were abundant in those parts where the increased vascular supply was found, and spindle cells were also more abundant here, and were often found arranged either parallel or concentrically to the lumen of the vessel.

The exciting cause of death in this case was the injury received about a fortnight previously. The history of the patient further shows that her mode of life was such as to produce kidney disease. For the completeness of the case it is to be regretted that the microscopic examination of the urine was not more successfully carried out, but with the aid of the post-mortem record nothing is needed to classify this case along with the others, as one showing advanced renal disease.

The microscopic examination of the kidney showed that the organ was to a marked degree contracted, and that the change was of considerable duration. The interstitial process, however, had not subsided or was perhaps rekindled to greater activity as the result of the injury from which the patient had suffered. The epithelium of the tubules was in the condition usually found in kidneys of this character; in parts where the contraction was marked the cells were greatly degenerated or had wholly disappeared, whilst in others where the connective tissue changes were less advanced the epithelia were often found well preserved.

The renal ganglia, in this case, presented marked evidences of degenerative changes of its ganglionic cells. The connective substance of the nervous masses showed decided formative activity of its cellular elements; the vascularity was greatly increased.

Case IV.—Adolph L., æt. 50; married, gasfitter; was admitted to the hospital September 19, 1878, in an unconscious condition. But shortly consciousness partially returned, and when asked his name he said L., yet this was the only response in words that could be gotten from him. No history could be obtained of his previous condition. Both pupils were

tightly contracted. Respiration 24; pulse 90, full. Twitchings of the muscles of the left side of face were noticed; the right side of the face was paralyzed. His mouth was drawn somewhat to the left, and on protruding the tongue its tip deviated to the right. The right arm and leg were paralyzed. The urine was cloudy, acid, sp. gr. 1009. It contained about one-sixth its bulk of albumen.

20*th*. General condition about the same; intelligence improved; he muttered when spoken to, but no words could be distinguished. He was rather restless in bed, and had passed his urine and feces unconsciously. Swallowed fluids with some difficulty. His chest was full of coarse mucous râles. No cardiac murmurs were heard. The superficial arteries were noticed to be very tortuous.

21*st*. His condition about the same. A microscopic examination of his urine showed that it contained great numbers of highly granular and fatty casts, as well as hyaline and oil casts, free fat globules, and fatty and granular renal epithelium. Respirations 48; pulse 160.

22*d*. Respirations 42; pulse 168. Total paralysis of sensation and motion over the right half of body. Death at 11 P. M.

Post-mortem examination, by Dr. Longstreth.—*Head.*—Calvaria normal. The dura mater was found tightly adherent to the bone and in places to the convexity of the brain. At the base, the vessels were markedly atheromatous. The left lateral ventricle was filled with black clots of blood, which came from an extensive laceration of the optic thalamus. The *cavities* of the body presented nothing especial.

Heart.—Weight 12 oz. avoird. Its left side was firmly contracted; its right side was distended with clots. The aortic valve was competent, but both the aortic and mitral valves were atheromatous; their surfaces were smooth. The left ventricular cavity appeared of smaller size than normal, and its wall was thickened, especially towards the base. The *lungs* showed deep posterior congestion.

Kidneys were much reduced in size; the left one weighed $2\frac{1}{2}$ ounces; the right 2 ounces. They were of a pale yellowish colour, rather flabby in consistence; their capsules thickened, not tightly adherent, and after removal left the surface of the organ finely granular. The cortex was much reduced in thickness, although its thickness in proportion to the length of the medullary cones, was less altered than is usual in kidneys so much reduced in size. They had a strongly urinous odour.

Microscopic Examination of the Kidney.—The surface was uneven and irregular in outline, but not markedly granular, although at places granulations were visible. The capsule was moderately thickened, loose in structure and not strongly adherent to the surface of the organ. Several large vessels were seen in it, and the remains of numerous small ones; and the lymph spaces were large and filled with a granular debris. Beneath the capsule were a number of cysts not larger than Malpighian bodies. The connective tissue of the capsule was encroaching on the cortex, and several of the Malpighian bodies were involved in its deeper layers. The walls of the bloodvessels were only moderately thickened, the increase being due to swelling of their tissues. The connective tissue surrounding them was of loose character, and the middle layer showed its muscular fibres very indistinctly, and this portion exhibited marked granular degeneration.

The capsules of the Malpighian bodies appeared as broad bands of swollen connective tissue, nearly devoid of cellular elements. These cap-

sules did not show as well defined, firm connective tissue directly encircling the capillary tufts as in many of the other specimens, but as a loose tissue extending diffusely into the surrounding area, and involving and destroying the neighbouring tubules. Very many of the Malpighian bodies appeared as homogeneous structureless masses, very granular in character and pigmented; in others, the capillaries showed distinctly, but not injected, and were surrounded by a slightly increased connective tissue.

The convoluted tubes were irregularly swollen in some places and contracted in others; many tubes were stripped of their cellular lining, empty and collapsed. Their basement membranes were swollen and thickened, and in many places fused with the surrounding overgrowth of connective tissue. The epithelial cells were highly granular and fatty; their nuclei were, as a rule, not visible, and the whole group of cells lining the tubules were swollen. The lumina of the tubules were choked with casts of great variety of structure; though mostly granular and fatty. The straight tubes of the medullary cones were much altered; their epithelial linings were indistinct, and very many of them were filled with casts.

The connective tissue of the cortical portions was greatly increased; the spaces between the tubules were widened, the tissue fibrillated and granular, and mostly devoid of cellular elements. In many places the encroachment of the intertubular connective tissue and the collapse of the tubules had converted the cortical substance into a mass of striated fibrillar tissue, in which holes of small size filled with granular detritus, were seen.

A general survey of the cortex showed that in about one half of it the tubules, with their degenerated epithelium in position, were intact, and that in the other half the connective tissue overgrowth, itself in a highly granular condition, had encroached upon and destroyed the tubules and Malpighian bodies, so that only their remains could be detected.

Microscopic Examination of the Renal Ganglia.—The ganglia were surrounded by thick, firm, connective masses, very abundantly vascular, and containing a moderate amount of adipose tissue. The connective tissue was especially abundant around the nerve trunks at their points of exit, and was unusually noticeable in the interior of the nerves.

The ganglion cells presented a confused, indistinct, and smeared appearance; they were very distinctly isolated from their surroundings, but their outline was irregular, and the cell bodies looked as though shrivelled. This condition was more marked in the more central portions of the ganglion, while towards the periphery many cells were more plump and rounded. The substance of the cell bodies appeared degenerated, although the granular and fatty changes in them were not as distinctly visible as in many of the other cases; in the stained specimens the tissue appeared like a blot of colour without definite structure. The nuclei were mostly very indistinct, and appeared blended with the cell body. The nucleolus, however, was very frequently discernible as a dark dot.

The tissue of the ganglia was strikingly altered. It was mostly composed of a coarse, firm, connective-tissue substance, in which were seen a moderate number of small round cells or nuclei and spindle cells. These cells, especially the round ones, were highly granular and not perfectly rounded, and the spindle-shaped ones were being converted into fibres. They stained very imperfectly. In the central portions of the ganglia this connective tissue was firmer and coarser, and was arranged so as to form cleared spaces concentric to the ganglion cells.

The vascular supply within the ganglia was scanty, and was carried on

by relatively large capillaries, surrounded by considerable firm connective tissue; numerous collapsed capillaries were also seen. The large vessels were injected, and several small hemorrhages were found near them, both at the periphery and in the interior of the ganglionic masses. Study of the condition of the capillary walls was impossible on account of the presence of the blood corpuscles within the vessel.

The history shows the condition of degeneration present in the greater portion of the arteries, and that the patient was suffering from chronic Bright's disease. His death resulted from cerebral hemorrhage, which is so frequently a consequence of contracted kidney. The autopsy records that the kidney had suffered at a period considerably prior to death, from interstitial inflammation. The much reduced size of the organs is, however, not entirely due to the contraction of the intertubular inflammatory tissue. This change had caused its usual effects in the tubular epithelium, and this portion of the organs had become markedly degenerated. The disease of the arterial system had contributed largely to the atrophy and degeneration found in all parts of the organ. The alterations in the kidney are, therefore, to be looked upon as due largely to atrophy and not solely to contraction. The interstitial inflammation was the first step in the morbid changes; the tubular epithelium suffered from the effects of the contraction of the inflammatory products, and both of these structures were further altered by atrophic degeneration caused by the atheroma of the arteries. That this interpretation of the condition of the kidney is correct, is evidenced by the flabby consistence of the organ as compared with its reduced size and weight.

The appearances of the ganglia prove that their connective tissue capsules are thickened, and that the changes in the periphery are accompanied by similar connective tissue hyperplasia in the interior, the fibres of which are coarse and firm, and there are present in this tissue new cellular elements, some of which are passing into fibrillar tissue, some or most of them are degenerating. The ganglionic cells are degenerated also, more particularly in their nucleus and nucleolus. The condition of the capillaries is also striking; the increase of connective tissue around their walls, and the evident degeneration of their tissue, evidenced by the occurrence of small hemorrhages, are especially to be noted.

Case V.—Wm. S. E., æt. 54, manufacturer, admitted to the Pennsylvania Hospital, March 6, 1878, in a nearly comatose condition, was unable to speak, but pointed to his pocket where letters were found directed to him. There was almost complete loss of power of his right arm and leg, the face was flushed, the conjunctival vessels were injected, and his pupils contracted. The first sound of the heart was heavy, the pulse regular, slow, and full. The radial arteries were markedly atheromatous. Later, he was able to speak a little, and made the statement that he felt well on leaving home in the morning, and while walking along the street became faint and fell unconscious. No further history could be obtained from the patient, partly from his stupid condition, but more especially on

account of his difficulty in speaking. The next day he was more intelligent, but his speech was very thick.

8th. Rather duller. Bowels opened by purgative. The urine was passed involuntarily; the small amount collected was opaque, yellow-coloured, alkaline, sp. gr. 1017, and contained albumen. With caustic potash, the urine became thick, viscid, and stringy. No casts were found on superficial examination with the microscope; the determination of their presence was, however, very difficult, owing to the thick sediment. He died on the eighth day without striking changes of the symptoms.

Post-mortem examination, by Dr. Longstreth.—*Head.*—A large clot of blood, which originated from the left optic thalamus, filled the left lateral ventricle. The walls of the cerebral arteries were atheromatous.

Cavities.—The *peritoneal* and *pleural* cavities presented nothing especial to note. The *pericardium* contained a small amount of blood-stained serum, its vessels were injected, and there was a very fine layer of lymph on its surface.

Heart.—Right side relaxed, left moderately contracted; its cavities nearly empty. Its orifices were normal in size, and its valves competent. Coronary arteries rigid and atheromatous. The commencement of the aorta was slightly dilated, and showed marked atheromatous changes, making its surface uneven. The mitral leaflets were atheromatous, but presented a smooth surface. The aortic valves were not changed. The cavity of the left ventricle was of normal size, its wall measured, at mid-ventricle, $1\frac{1}{2}$ inches in thickness, towards the apex much less. The muscular tissue was rather flabby but resistant.

The *lungs* were emphysematous anteriorly, whilst posteriorly they showed deep congestions. The *spleen* was small, firm, had a nodular feeling. On section, the nodules appeared like areas of infarction. The *liver*, *stomach*, and *intestines* presented nothing especial to note.

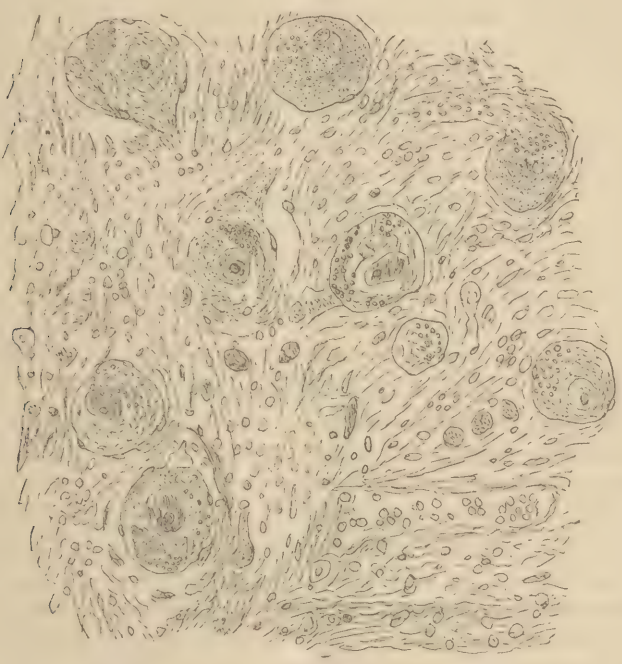
Kidneys.—The left was small, not very firm, and slightly irregular in its outline. The capsule was opaque, thickened, and adherent, and on removal tore the tissue of the organ and left a highly granular surface, on which the stellate veins were distinct. The cortex was found much reduced in thickness, and its tissue was opaque and mottled. The organ had a distinctly urinous odor. Weight three ounces. The right kidney presented the same general characters. The bladder mucous membrane was swollen, and probably in a state of catarrhal inflammation of slight degree. Urethra not examined.

Microscopic Examination of the Renal Ganglia.—The connective tissue capsule of the ganglia was found moderately thickened and firm in parts, and contained within its meshes numerous cellular elements. The adipose tissue in it was abundant, and the vessels were not numerous, but some had very abnormal walls.

The ganglionic cells were irregular in their outline, some appearing shrivelled; their structure was markedly indistinct, and they contained abundant granular and fatty matters, and some also considerable pigment granules. Their nucleus was generally invisible, or some portion of its outline was invisible, from the accumulation of granules or fat. The nucleolus presented a dark outline or a black spot; it was rarely bright or shining. The connective substance of the ganglia had a coarse, highly granular or even fatty, striated, or fibrillated appearance. There were numerous cells in it, in some portions nearly all rounded, but of highly granular aspect, in other portions numerous elongated cells. These cellu-

lar elements stained imperfectly, and were faint or indistinct. The vascular element in the nervous masses was poorly represented in quantity, but the vessels seen in it presented marked thickening of their walls; there was hypertrophy of the muscular coats to a considerable degree, and of the connective tissue around them.

Fig. 3.



The ganglia cells are changed in outline, show many oil-globules, the nuclei form black dots or outlines. The connective tissue is fibrillated and contains very numerous new cellular bodies. × 350.

The atheromatous condition of the superficial vessels and the cerebral hemorrhage both indicated degenerative changes in the internal arteries of the body.

The microscopic sections of the kidney were spoiled through some defects in the mounting. Sufficient, however, is known of the minute appearances to enable us, in connection with the evident alterations seen by the naked eye, to classify this case with the others. The kidney showed atrophic changes as well as marked evidences of contraction and of degeneration of the epithelium.

The degeneration and atrophic changes in the ganglia were very evident both in the ganglion cells and the connective substance. It is also evident that at some period active changes were present in the latter constituent. The muscular coat of the arteries was altered in this case in the way which has been described in so many of the previous ones.

In group II., the group just described, the life history and the condition of urine and kidneys, show that either the renal disease was of a somewhat different type or that it was less advanced. In the first case the patient had led a life strongly predisposing to kidney disease; the kidneys were of the contracting variety, and the slightly swollen condition noted at the autopsy probably resulted from intercurrent, subacute changes brought on as the result of her recent injury. In the second case of this group, we have no report of the condition of the patient previous to admission; death was due to cerebral hemorrhage. The kidneys were greatly contracted, but the microscopic examination, as well as the general condition of the organs, shows that marked parenchymatous changes existed in addition to the interstitial disease. In the third case the death resulted from cerebral hemorrhage also; the life history is exceedingly brief, and fails to indicate with any positiveness the existence of renal disease, and for this reason we have hesitated to include the case in this list. But so evident is it from the autopsy and examination microscopically of the specimens that kidney changes had been going on for a long period, that we have concluded to give the case along with the others with which it in other respects closely agrees.

In this group the renal ganglia are found strikingly altered, but to a different degree from those in the previous one. The adipose and connective tissues around the nervous masses, as well as around the kidneys, show similar changes to those already spoken of. The ganglionic cells are in all these cases markedly degenerated, but not to an equal degree to those in group I. The most striking difference between these cases and the previous ones is seen in the condition of the connective basis substance of the nervous masses. These cases all agree in showing this tissue filled to a greater or less extent with small cellular elements, having the usual characters of connective-tissue elements. In the previous group, as already pointed out, the active hyperplastic changes in this tissue were considered to be subsiding; the cellular elements had passed on to the formation of fibres, although a few were still to be seen. In this group of cases the cellular elements are in great abundance, some presenting themselves as round nuclear bodies, others as spindle-shaped cells, but the contractile changes of this tissue are much less marked than in the previous group. The display of vessels in and around the ganglia is very prominent, and is in co-ordination with the progress of the histological alterations of the morbid process, and in correspondence with the relative advance of the kidney changes.

Yet another group presents itself for examination, and in this *third group* we have more of the clinical features as well as the pathological changes in the kidney of catarrhal inflammation, mostly of the acute type, and we shall find the disease in the ganglia much less marked.

Case VI.—Charles O., æt. 28, single, bartender, was admitted to the hospital on Wednesday, February 6, 1878. He had always been in good health, but had been a hard drinker. On Sunday previous to his admission he awoke with a severe headache, having gone to bed the night before well. This condition continued, and, on the day before admission, he was seized with a chill, followed by vomiting, and was obliged to go to bed. He was very restless that night, and evidently feverish. He was constipated, and complained of loss of appetite, bad taste in the mouth, and his tongue was coated and dry.

On admission, the patient, who was very stout, presented a red, much swollen, markedly erysipelatous face. His temperature was 107° F.; in the evening the thermometer registered 104° F.

The next morning he was very restless, nauseated, tongue swollen and blistered. Temperature 107° F. His urine was cloudy, orange-coloured, acid, specific gravity 1020; it contained a considerable amount of albumen, and the microscope showed hyaline and granular casts.

8th. Complained of pain in back and limbs. The erysipelas spreading. Temperature 104° F.; pulse 146 per minute; extremely delirious. Tongue dry and very much furred. His hands were cyanosed.

9th. Very restless and delirious. Respirations had become stertorous during the past night; face livid and swollen. The urine was of a light claret colour, acid; specific gravity 1018, and contained about one-sixth its bulk of albumen. Died at 8.15 A. M.

Post-mortem examination, by Dr. Longstreth.—*Cavities.*—The *peritoneum* was injected, but without lymph. Many old adhesions of the *pleura*. The *pericardial* sac contained a little clear serum; the vessels on its surface were injected.

Heart.—Its right side was relaxed, and filled with blood and clots; its left side was contracted. Both the aortic and mitral valves showed morbid changes; the anterior flap of the mitral was thickened, and two of the aortic leaflets were adherent for a short distance near their insertion, and were thickened and opaque at deeper portions, and thinned in places near their free margins, almost to perforation. These changes were of old date. The whole of the endocardium of the left ventricle was thickened and opaque, and the left ventricular wall was hypertrophied.

The *spleen* was large; it showed several old infarctions of small size.

The *liver* was enlarged, moderately firm; its surface granular.

The *kidneys* were large, swollen-looking, smooth on the surface, and of regular outline. The stellate veins were very conspicuous, the capsule was tightly adherent and thickened. The cortical portion of the organ was much increased in thickness; its tissue presented a mottled, opaque aspect. The organs had a strongly urinous odor.

A microscopical examination of the kidney showed its tissues to be very much swollen. Its capsule, which in the fresh condition was tightly stretched over the swollen organ, and firmly adherent to it, was seen separated from its surface, and retracted at the sides of the section. The capsule was thickened, and composed of firm connective tissue; its vascular supply was inconspicuous, but its lymph spaces were large, and filled with granular and fatty matters, and some blood corpuscles. The larger vessels were enlarged, and their coats thickened, especially the outer coat; the muscular was highly granular, and its striæ indistinct. The Malpighian bodies were mostly large and swollen-looking; their capillary tufts appeared distended with blood corpuscles, but were greatly

obscured by the granular cell elements around them. Their capsules were thickened and swollen, and were composed of firmer connective tissue than normal. They were pressed upon, and even indented, by the swollen tubes and tissue around them.

The convoluted tubes were irregularly dilated, and their basement membranes thickened and swollen. Their epithelium was highly granular and fatty, the nuclei invisible, and the outlines of the cells very indistinct; so swollen were the cells that they apparently closed the lumen of the tube. Many of the tubules were filled with blood-clots, in which, however, the blood corpuscles could not be distinguished. So frequent was the occurrence of these hemorrhages, that under the lower power (1 inch ob.) in many fields of the microscope, four or five tubes thus filled with blood could be counted.

The connective tissue between the tubules was markedly swollen and loosened, yet its amount and its firmness were increased above the normal. The swelling of the tissue was so great, and the presence of cellular and blood corpuscles so abundant, that it was not possible to state whether contraction of the organ had taken place previously to the acute process. No collapsed or shrunken tubules could be made out.

The capillaries were everywhere distinctly visible by their contents of blood corpuscles. These corpuscles varied in amount from a single row to masses consisting of several rows distending the vessel till it equalled the size of the tubule itself. The filling of the vessels equalled the picture presented by the most complete artificial injection.

Microscopical Examination of the Renal Ganglia.—The connective tissue covering the ganglionic mass was decidedly thickened, swollen, and firmer than normal; its vascularity was moderately increased, and considerable adipose tissue was present in it. It was firmly attached to the mass, and was encroaching upon and surrounding the ganglionic cells at the periphery; it was more abundant than normal around the nerve trunks, and penetrated with them into the interior.

The ganglionic cells were irregular in their outline, and generally did not show their structure with clearness and distinctness. Their substance was markedly granular, only slight fatty changes were visible, and the pigmentation was not conspicuous. In many of the cells the nucleus was obscured by the surrounding granular changes, but the nucleolus was distinct, appearing as a black outlined spot.

The connective substance of the ganglion presented a swollen, highly granular, and striated appearance, and was increased and firmer than usual, and the ganglionic cells appeared partitioned off in groups by bands. This tissue contained a considerable number of rounded and elongated cells, but they were in a highly granular condition, and stained but poorly. There was seen to be some retraction of the tissue around the ganglionic cells, yet the spaces were not wide, and frequently contained granular material or small granular cells. The nuclei of the ganglionic cell-walls showed in some cases very distinctly.

The capillaries in the interior of the ganglia were conspicuous, and usually filled with blood corpuscles; in many cases they appeared of large size, and over-distended; but others were seen which had thickened tissue around them, and were evidently shrivelling; no hemorrhages were visible.

This patient was admitted with a severe attack of erysipelas, from which alone it is not probable that he would have succumbed had his

organs, especially the kidneys and liver, not already been affected by morbid changes. The urine contained a very considerable amount of albumen, and the microscopic examination of it, made only once, showed cylinders of a clear glassy appearance, inclosing, however, very many small granules. It is probable, from the colour of the urine, and condition of the kidney as exhibited by the microscope, that on the last day blood and epithelial casts would have been found.

The microscopic appearances of the kidney, taken in connection with the drinking habits of the patient, show that the organs were diseased prior to the attack of erysipelas, and this change consisted in a slight alteration of its vessels, and an increase of its connective-tissue constituents. It is probable, also, that the epithelium was also affected, as the renal phenomena were in excess of those usually seen in cases of uncomplicated erysipelas, though albuminuria of moderate or slight amount is the rule in this condition.

In the renal ganglia the changes were of moderate degree. The ganglion cells were granular, but not fatty. The connective tissue was increased in amount, and firmer than usual, but the cells of this tissue showed but slight active changes. The vascularity of the nervous masses was increased.

Case VII.—James E. K., coloured, æt. 29, was admitted March 25, 1878. The patient had suffered from intermittent fever many times during his life, but was never confined to bed by the disease; and did not think his general health was materially impaired thereby. During the last year he had been perfectly free from it, and had been well until five weeks before coming to the hospital, when he noticed a change in the secretion of the urine, and that he passed apparently more than usual; he became dull and listless; had some headache. Two weeks later his eyelids and face began to swell, afterwards his lower extremities, and finally his whole body became œdematous.

The urine was of pale yellow colour, acid, sp. gr. 1017; with heat and nitric acid there was precipitated about two-thirds its bulk of albumen. The microscope showed granular, epithelial casts in great number, and some hyaline and blood casts, together with free blood corpuscles. On the 1st of April he suffered from severe pains in both shoulders with increased temperature (104·5° F.), also from great tenderness to pressure over nearly the whole body, and severe pain in the lumbar regions. The general œdema decreased, and the pains lessened. On April 8th there was a failure in the secretion of urine, and shortly afterwards an abundant effusion occurred in the pleural cavities and pericardium. On the 17th of April the right leg was red and painful, and a day or two later it presented the appearance of erysipelas; subsequently an abscess formed at this part, and on two occasions large amounts of pus were withdrawn by aspiration. He gradually lost strength, the dyspnœa increased, respirations were 40 per minute. The condition of the urine remained about the same, the casts later were mostly granular and fatty. The patient died May 11, 1878.

The *autopsy* showed a large amount of inflammatory effusion in the *left pleural cavity;* over the upper part of the lung the pleural surfaces were

firmly adherent. The *right pleural sac* held less inflammatory material than the opposite side, but the lower lobe of this lung was markedly compressed. The *pericardium* contained a large quantity of serum and lymph. In the *abdominal cavity* was considerable serous effusion, but the peritoneum showed no evidences of inflammatory action. The valvular apparatus of the heart was normal, and its muscular tissue presented no marked alteration, except at the pericardial surface.

The kidneys were large and swollen; their outline was regular and their colour pale. The general appearance was such as usually characterizes the second stage of acute Bright's disease of the catarrhal type.

The other organs showed nothing especial to notice.

Microscopic Examination of the Kidney.—The surface of the *kidney*, as seen in the microscopic section, is smooth and regular. The capsule presented a swollen, loose appearance, but there was no increase in the firmness or the amount of its connective tissue. Its vascularity was not augmented; its lymph spaces contained considerable granular matter.

The lumina of the large vessels at the base of the pyramids showed smaller openings than usual, and were evidently pressed upon by the swollen tissue around them. Their internal coat was much folded and puckered, but the middle and external coats were not altered, except by a moderate swelling of the connective tissue at the periphery of the vessels. The Malpighian bodies appeared swollen and enlarged; some of them showed their capillary tufts injected, others were empty and their cellular elements were highly granular and fatty. Their capsules were swollen and wider than normal, but the connective tissue was loose, and not increased in amount; in some were present granules and fatty matter.

The epithelium of the convoluted tubes was generally highly granular and fatty, and so swollen that it nearly or quite closed the tube; in other tubes, a much smaller number of the epithelial cells presented more nearly normal conditions, and were evidently newly developed, having relatively large nuclei. The nuclei of the majority of the cells were greatly obscured by the granular and fatty changes which had taken place. Many of the tubes were clogged with granular and fatty debris. The basement membranes of the tubules were everywhere swollen and irregularly distended, and the interspaces between them were widened and the connective substance highly granular, but not increased in amount or firmness. The capillaries in many parts were injected with blood corpuscles, but in other parts were empty, the one or other conditions depending on the presence or absence of the swollen cells within the tubules.

It was evident from a general survey of the cortex that its thickness was increased, and that this swelling was so great that the capsule was much stretched. In some parts of the cortex the acute process had subsided, and the degenerated epithelium of the tubules was being replaced by new elements; in other portions the tubules were still clogged by degenerating cells and inflammatory products. In some parts the circulation was returning to its normal condition, or was even in excess, and in others it was hindered by the morbid condition of the tubular epithelium and of the adjacent parts. In the tubes of the medullary cones numerous fatty and granular casts were seen occupying a portion of their length; in this part the bloodvessels were greatly overfilled with blood, and here, too, the connective tissue between the tubes was swollen.

Microscopic Examination of the Renal Ganglia.—The connective tissue surrounding the ganglion mass was comparatively of small amount, loose

in character, and slightly connected with the nervous tissue, and was much less firm and coarse than in most of the other cases. It appeared somewhat swollen and œdematous, and where it passed into the substance of the ganglion around the bloodvessels, or accompanied the nerve trunks especially, its cellular elements were increased. There was also an increased amount of adipose tissue found in it.

The ganglionic cells showed distinctly and clearly, unobscured by the changes around them, or in their interior. Many of them exhibited double nuclei and nucleoli; about two-thirds of the cells presented no alteration, except an increased granular change with an occasionally visible fatty granule, whilst the other third were markedly granular and fatty, especially around their single nucleus, which, in these instances, was nearly or quite invisible.

The tissue of the ganglion had a finely granular, somewhat striated appearance; at no part were there any coarse fibres, or any penetration of the ganglion mass by the ingrowth of connective tissue bands from its capsule. The basis substance showed a moderate number of small round cells scattered through it, and a fewer number of elongated ones. There were no cleared spaces around the nerve-cells as witnessed in other specimens. In general, the aspect was that of an evenly spread basis substance, having numbers of small round or spindle, strongly stained cells scattered through it, and in which the plump and regularly rounded ganglion cells rested as in a bed. Vascularity and injection of the vessels, both at the periphery and in the interior, were deficient in a very striking degree.

This patient suffered from catarrhal (parenchymatous) nephritis, which in the early stages was of a mild type and rather slow in its advance. The symptoms were noticed five weeks before his admission to the hospital, and during this period he was without proper care. The progress of the disease was unfavourable, being complicated with pericarditis and pleurisy and with abscess of the leg. At the autopsy the kidney presented the appearances usually seen in the large white kidney of Bright or in Grainger Stewart's second stage of acute nephritis. The microscopic examination of the organs showed a swollen condition of the connective tissues. The vessels and the connective-tissue portions of the organ showed only such alterations as are dependent on acute disease. The epithelial cells of the tubules were highly granular and fatty, and to these elements the morbid changes were principally confined. The casts in the tubes were of the same character as those in the urine during life. The ganglion cells in this case were comparatively little altered; in the connective substance of the nervous masses, there was no fibrillation of the tissue, and the cellular elements of this part were but little increased in numbers and showed but slight hyperplastic or formative changes.

Case VIII.—Sabilla R., æt. 16, coloured, single, domestic, admitted to the Pennsylvania Hospital January 26th, 1878. The patient had always been healthy until two years previous, when she had an attack of rheumatism, affecting the ankles and knees; this attack was not so severe as to confine her to bed, but since she has noticed slight palpitation of the

heart from exertion. The previous winter she has been much exposed to cold and wet. Nine days before her admission slight pains in the ankles began, and six days ago almost every joint of the body was painful, and in addition she has had pain in the cardiac region and dyspnœa, and has gradually grown worse.

On admission, her temperature was 105° F., pulse 136 per minute, respiration 72, panting and shallow. There was some pain and a little swelling of both hands. Owing to the rapidity of the heart's action, its physical examination was difficult and uncertain; there seemed to be an apex systolic murmur and a friction sound over the body of the heart, confined to a very small area. The heart appeared displaced.

Urine note. Jan. 27.—Cloudy, acid, sp. gr. 1010, albumen in small quantity. The microscope showed pus (?) corpuscles, squamous and pavement epithelium, and a few granular and hyaline tube-casts.

The patient gradually sank and died Feb. 5th, death being preceded by marked evidence of a pulmonary complication.

Post-mortem examination, by Dr. Longstreth.

Cavities.—Considerable serum was found in the *abdominal* cavity, containing large masses of fibrin. No evidence of peritonitis. The *pleural* cavities showed numerous old and recent adhesions, serum and flocculent lymph, especially at right base.

The *pericardium* was distended with serum and recent lymph; the lymph was half an inch thick, pretty firm in character and adherent to both the surfaces.

Heart.—The right side distended, the left firmly contracted. Both the mitral and aortic valves showed numerous recent vegetations of small size along the line of contact of their leaflets, which were swollen and opaque. The heart weighed 12 ounces av.; its left ventricular wall measured $\frac{3}{4}$ inch in thickness.

The *lungs* were compressed by the pleural effusion, and there were areas of pneumonic consolidation in the right lower lobe.

The *spleen* showed several small, recent embolic patches.

The *kidneys* were not much enlarged, appeared swollen, and were of doughy consistence. The capsule was slightly thickened and more firmly adherent than normal, but on removal left a smooth surface, showing the stellate veins distinctly. On section, the cortex was swollen and increased in thickness. It was homogeneous looking and opaque.

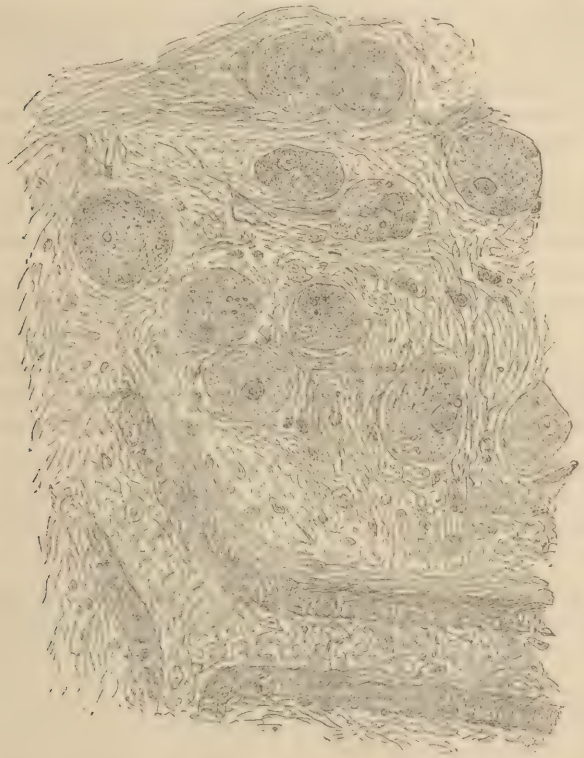
The microscopic sections of the kidney from this case were lost, and a particular description of it cannot therefore be given. The condition present was that of cloudy swelling of the tubular epithelia and also an increase of the intertubular connective tissue. The microscopic examination was carefully made at the time of the autopsy, but as the specimens were lost we have only appended this short note of the condition of the kidney.

Microscopical Examination of Renal Ganglia.—The connective-tissue covering of the nervous mass was considerably thickened, composed of firm bands, swollen and contained considerable adipose tissue. The vessels in it were larger and more numerous than normal, their coats thickened, especially the muscular layer, but they were empty of blood.

The ganglionic cells were pretty regular in their outline, though perhaps generally less so than those represented in the drawing; many were quite irregular, looking notched and shrivelled. They were mostly highly granular, and many showed fatty changes. The nucleus was as a rule dis-

tinct, although obscured by the changes in the cell-body; but occasionally it was either quite invisible or some portion of its outline was lost. In some of the nuclei black granules were present. The nucleoli showed distinctly as black outlined circles or as black dots.

Fig. 4.



The cells are regular in outline, show much granular change and a few fatty particles. The connective substance is swollen and firmer than normal, and only a few new elements are present. The arteriole has its muscular coat hypertrophied and the connective tissue around it is increased. × 350.

The connective substance of the ganglia presented a loose, swollen appearance, its fibres were moderately coarse and loosely collected, but they passed band-like through the nervous mass and partitioned off the cells more or less completely into irregular aggregations. Its tissue was highly granular in places, in other parts between the fibres was a hyaline basis material, which, especially around the vessels, gave an appearance not unlike myxomatous degeneration, although the condition was evidently not of such character. A moderate number of cells were present in it, both rounded and elongated, which stained but poorly and were mostly granular and fatty. The vascularity of the ganglia was obviously increased. Numerous capillary vessels were present having thick swollen walls or surrounded by an increased amount of connective tissue. Some of them were dilated, others were collapsed. They were empty of blood, and no hemorrhages were seen.

We think it may be concluded that the clinical record of the urine shows that the patient had suffered from renal disease previously to the time of her admission with the acute illness of which she died. In fact, it was a question during life whether the pericarditis and pleurisy were not of renal origin. Although the patient's story on admission indicated an acute attack of rheumatism, the symptomatic evidence of it was not strong, and by far the greater difficulty under which she laboured was the pericarditis, combined with pleuro-pneumonia. The condition of the kidney is confirmatory of the clinical evidences of renal disease prior to her last illness. That albumen should be present in the urine and that cloudy swelling of the tubular epithelium should result from the high temperature are not unexpected conditions. But the thickened capsule and the increase of the intertubular connective tissue show that previous disease had existed in the kidney.

Some of the alterations found in the ganglia were the results of such changes as come to all the tissues of the body in acute diseases attended with high temperature. The swollen condition of some portions and part of the granular changes are to be interpreted in this manner. In addition to these, we have irregularity of outline, a marked granular and a fatty degeneration of the ganglion cells. The increased cellular elements in the connective substance of the ganglia and increase of the fibrous and connective tissue, both in the periphery and in the interior of the nervous mass, show changes not due to any acute process.

Case IX.—Mary W., æt. 26, coloured, married, domestic, admitted to the Pennsylvania Hospital, November 12th, 1877. Her father died of consumption; her mother of "dropsy." The patient had always been healthy; she had been married six years and had one child. Two months previous to her admission to the hospital, she had a severe attack of "biliousness," for this she took a strong cathartic, which produced a very free diarrhœa, and to this she ascribed her illness. Soon after this time she began to complain of malaise, headache, loss of appetite, and nausea, all of which gradually increased, and during the latter part of the month prior to her admission she was compelled to give up her work. About this time, she had a continual diarrhœa, and a cough began, attended with abundant mucous expectoration, which soon became blood-stained. Up to the time of her admission she had had no œdema of the feet or other symptoms of kidney disease; she had previously been much exposed to cold and wet.

On admission, there was considerable fever, no hebetude, tongue coated with moist whitish fur. Abdomen not tympanitic, considerable diarrhœa, the passages of a very fetid character, no vomiting. Cough with bronchitic blood-stained expectoration, resonance over both lungs not impaired, mucous râles on both sides posteriorly and on the left anteriorly.

Urine, clear, yellow, acid, specific gravity 1021. Albumen in small amount and numerous granular and hyaline tube-casts.

14*th*. Temperature 105° F.; some dyspnœa. Impairment of resonance at right base, other phenomena the same.

16*th*. Expectoration contained more blood. Hebetude and subsultus tendinum.

18*th*. Expectoration less bloody. Diarrhœa and other phenomena continued the same. Subsultus increased. Slight delirium. Urine scanty. Temperature 105½° F.

19*th*. Urine contained one-eighth albumen, specific gravity 1020. Large amount of epithelial cells and granular tube-casts and some free oil globules. Subsequently, the condition of the urine was not to be accurately determined, as the patient was delirious and emptied the bladder involuntarily, but the amount increased. The physical signs in the lung indicated a catarrhal pneumonia. The diarrhœa continued. The diagnosis was typhoid fever and catarrhal pneumonia. Died, November 24th, 1877.

Post-mortem examination, by Dr. Longstreth.—*Cavities.*—The *peritoneum* was smooth, no increase of serum and no lymph or recent adhesions. The *pleura* and *pericardium* showed nothing especial.

Heart.—Right side distended and relaxed, and contained large firm clots; the left ventricle flabby and empty, and slightly dilated. The mitral valve showed a spot of atheromatous degeneration, and the commencement of the aorta showed similar changes. Weight, 8½ ozs.

The *lungs* showed the characteristic changes due to catarrhal pneumonia. *Spleen* was small, its consistence flabby, pale, its tissue soft. *Liver* was swollen, moderately congested, its tissue less resistant than normal, and appeared opaque and homogeneous (cloudy swelling). *Intestines.* Several of Peyer's patches were deeply excavated. The mesenteric glands near by were enlarged and surrounded by an area of congestion.

Kidneys large, smooth, swollen looking, and their consistence was flabby. The veins on their surface conspicuous. The cortex was greatly thickened, opaque, and mottled; the capsule somewhat swollen, easily separated, and leaving the surface of the organ smooth and regular. The kidneys had a markedly urinous odour. Their structural parts presented microscopically nothing of note, except the tubules and Malpighian bodies.

All the parts of the organ were much swollen. The Malpighian tufts, with their cellular elements, closely filled the capsules; the cells were very highly granular, and prevented the recognition of the capillaries. A few blood corpuscles, however, could be distinguished in the tufts. The basement membranes of the tubules were swollen, and the tubes were irregular in outline. The epithelial cells, mostly retained in position, were very highly granular and fatty, and so swollen that they nearly filled the lumen of the tube; their nuclei were generally invisible. Many tubes were clogged with granular and fatty matters, or oil globules.

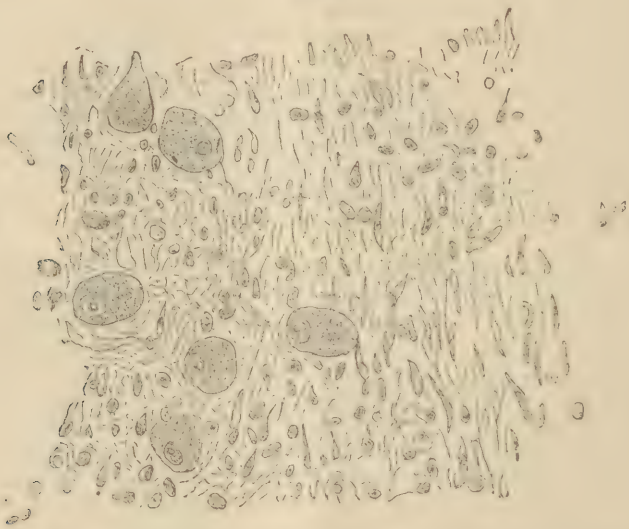
Microscopic Examination of Renal Ganglia.—The connective tissue envelope of the nervous mass showed little or no evidence of any abnormal condition. It was composed of fine, loosely matted fibres, devoid of adipose tissue; it exhibited no abnormal vascularity, nor its vessels changes of their coats. There was no increase of connective-tissue cells, and no increase of connective tissue about the nerves either along their trunks or at their entrance, or within the ganglia.

The ganglion cells were distinct, of regular outline, and showed but little evidence of structural changes. Their bodies were mostly free from granular or fatty alteration, and but little pigment was noticed within them. Their nuclei were always distinctly seen, although in numerous instances a few granules were seen within them or on their border. The nucleoli were clear and shining.

The connective substance of the ganglia was considerably altered,

though to a very much less degree than in any of the other cases. It was composed of a clear, transparent, very slightly granular and barely visible finely striated basis substance, in which were seen a considerable number of mostly elongated bodies and a few rounded cells. These elements were exceedingly delicate in their character, and not granular or fatty; they stained distinctly though not deeply. The nervous masses showed no aggregation of the ganglion cells, and no appearance of being partitioned off by bands or masses of connective tissue as was so distinct in many of the other cases. Doubtless many of the bodies depicted in the drawing were nerve fibres, and the cellular bodies were evidently of a recent character and exhibited no progressive changes. The whole structure was much more delicate than in the drawing.

Fig. 5.



The nerve-cells present more nearly normal aspects. The connective basis substance of the ganglia does not show any very distinct alterations; the cellular elements are increased, but some of those bodies are probably nerve-tubules and not new morbid products. × 350

From the history of the case, the pathology of the attack is not entirely clear; that she had typhoid fever, and that this was complicated with a catarrhal pneumonia, is quite evident. Whether the renal disease was of prior date, or whether coincident, is very uncertain. We are of the opinion that the kidney disease was of recent date. The fatty changes of the renal epithelium were probably produced through the influence of the profound blood changes due to the typhoid poison.

The renal ganglia were little altered, the principal appearance to be regarded as abnormal was in the connective substance of these bodies, and these changes were of recent origin, and they were very slight.

In group III. the type of disease is different from the cases in both the previous groups; albuminuria is a marked phenomenon, and the renal disease was not advanced, yet probably the immediate cause of death, except

in the last case. In Case VI., suffering from erysipelas, the evidence of pre-existing renal disease is plain. The condition of the kidney, as seen by the microscope, shows that interstitial changes had occurred previous to the incoming of the acute parenchymatous disease accompanying the erysipelas. These interstitial changes were not of such character as to produce contraction of the organ, or, at least in the presence of the tubular alteration, the contraction had been overcome and was not visible; the increase of intertubular connective tissue was however sufficient to markedly interfere with the renal functions, and this attack, which but for this condition, would probably have had a favourable issue, resulted in death. In Case VII. the history and the condition of the organs show a type of disease different throughout from any of the previous cases. The alterations in the kidney are those of acute catarrhal inflammation; there is slight disease of the bloodvessel walls, but no evidence of chronic interstitial changes. The case was complicated, however, with inflammatory disease of the serous membranes, phenomena much more common in connection with the contracted kidney than with kidneys presenting the type of disease which these organs exhibit. In Cases VIII. and IX., the evidence of kidney disease prior to the fatal attack is much less than in any of the other cases; and in Case IX. it can with great certainty be concluded that no renal mischief was present previous to about a fortnight before admission.

In this group, the changes in and about the ganglia were much less marked, or in some cases so slight as not to be appreciable; the connective-tissue increase and the accumulation of fat, both here and around the kidney, were noticeable conditions, and in respect to the ganglia is shown by the microscopic examination. In this group the ganglion-cells were markedly granular, but the absence of fatty degeneration separates the cases very distinctly from those in the previous groups. The condition of the connective basis substance of the nervous masses conforms to a recent hyperplastic alteration of this tissue, and corresponds to the recent or slightly marked changes found in the ganglion cells and with the type of the renal disease in this group. The vascularity here is likewise in correspondence with the tissue alterations.

In Case IX., the connective tissue alterations are very slight and are those due to acute conditions. The ganglion cells likewise show little alteration, and the basis substance is devoid of any evidence of contractile changes such as were seen in most of the previous cases.

We have thus, we think, by a series of cases arranged in different groups according to the prominence of the changes, proved that in Bright's disease the renal ganglia are materially altered, and we refer to the drawings for a verification of the statement.

The difficulty of the inquiry was considerable. We have searched carefully the sources from which we expected to derive information con-

cerning the microscopic appearances presented by the ganglia, without, however, obtaining much knowledge. A great deal has been written on the structure of the ganglionic cell, its nucleus and nucleolus, its nerve fibres, and its connection with the spinal system of nerves, as well as the fibres distributed from it, as a centre, to the various organs; and in giving our description of the condition of these bodies, the typical form, as shown by Bidder,[1] Arnold, Fräntzel,[2] Lubimoff,[3] and others, has been carefully held in view. But of the normal appearances presented by the tissue of the ganglia lying between the ganglionic cells, and in which these bodies rest as in a bed, and through which the nerve fibres pass to be distributed peripherally, we have found no satisfactory description and no plates which represent the normal condition. Key and Retzius,[4] however, have shown very beautifully the lymphatic spaces of the ganglia, and Ranvier[5] has studied minutely the condition of the nerve fibres. Of the pathological conditions of the sympathetic nervous system, Poincare and Bonnet[6] have described the changes occurring in general paralysis, Voisin[7] in certain psychical disturbances connected with disease of the abdominal organs, and Petrow[8] in constitutional syphilis. Lubimoff[9] has made the most extensive studies of the general morbid conditions occurring in the various divisions of the grand sympathetic and in the component parts of the sympathetic ganglia. Yet none of these authors, or any others who have worked in this field of research, have traced out any definite connection, in the relation of cause and effect, between the ganglionic changes and the morbid condition of any organ to which the affected ganglion stands in the relation of a nerve centre. Among the 250 cases in which Lubimoff examined the condition of the sympathetic, he mentions only two of kidney disease (nephritis diffusa), but gives no details of the cases or of the appearances presented by the ganglia, and does not connect the nervous changes directly with the renal disease. Our endeavour has been to discover whether anatomical alterations are to be found in the

[1] Die Nervi Splanchnici und das Ganglion Cœliacum. Arch. f. Anat., Physiol. und Wissenschaftl. Med., 1869, s. 472.

[2] Beitrag zur Kenntniss von der Structure der spinalen und sympathischen Ganglienzellen. Virchow's Arch., Bd. xxxviii.

[3] Embryologische und histogenetische Untersuchungen über das sympathische und centrale Cerebrospinal-Nervensystems. Virchow's Arch., Bd. 60 s. 217.

[4] Studien in der Anatomie des Nervensystems. Arch. für Mikroscopische Anatomie, Bd. ix.

[5] Recherches sur l'histologie et la physiologie des nerfs. Archive de Physiologie Normale et Pathologique, 1872.

[6] Recherches sur l'anatomie pathologique et la nature de la paralysie générale. Annales médico-psychologiques, 1868, p. 185.

[7] L'Union Med. 1872, No. 54, p. 650.

[8] Ueber die Veränderungen der sympathischen Nervensystems bei constitutioneller Syphilis, Virchow's Arch:, Bd. lvii. s. 121.

[9] Beiträge zur Histologie und pathologischen Anatomie des sympathischen Nervensystems. Virchow's Arch., Bd. 61, s. 145.

particular part of the nervous system directly connected with the renal apparatus, and what is the nature of this alteration.

We think it cannot be denied that a morbid condition hitherto not described has been shown to exist in the ganglia—a condition to be seen as distinctly with the unassisted eye as the abnormality of the kidneys themselves, and the microscopic examination of the ganglia has confirmed the existence of the changes and has shown that the histological alterations have been in some degree proportional to the amount and the duration of the kidney disease.

The question is then no longer as to the change, but as to its meaning. Is it simply consequence? is it part of a general degeneration which affects kidney and other parts of the body; or is it the starting point of the kidney disorder? Is it concomitant, is it cause? We do not think it consequence, for the alterations are discernible in the ganglia before any other tissues, except the kidneys, are markedly affected. Whether concomitant or cause is very difficult to answer. But we believe that it will be found to be the latter, at least for some of the forms of Bright's disease, and that the changes, especially in the type of the disease called interstitial nephritis, or contracted kidney, will be recognized to be linked to the changes we have indicated in the ganglionic cells, in the connective tissue and in the bloodvessels. Whether all forms, or to what extent the varied acute and chronic conditions classed under Bright's disease present these ganglionic changes and are dependent upon them, is a matter for future research; and we may, through this research, find an additional means of clear distinction between the renal maladies.

Speaking generally, and having more particularly the interstitial nephritis in view, we think that the physiological pathology of Bright's disease is to be interpreted in the following manner: the specific cause, whatever may be its unknown form or character, acts in such a manner on the ganglion cells, presiding as centres of innervation to the kidneys, and whose fibres distributed to the vessels of these organs regulate not only the calibre of the vascular trunks, by changing the state of contractions of their muscular fibres, but also probably the conditions of osmotic action between the blood and the renal tissues, that the collective phenomena, known as Bright's disease, are brought about. In the form of interstitial nephritis these phenomena present themselves as a condition of inflammation of the connective-tissue portions of the kidney, and with this change, we see the alterations of the muscular fibres of the arterial walls. The subsequent lesions in the kidney are the results of the further development of the inflammatory products and their cicatricial contraction, and are not the special effect primarily of the morbid condition of ganglion cells. The alterations of the connective basis substance of the ganglia, are probably of the same nature as the hyperplasia of the connective tissue of the kidney, and like this tissue, it undergoes similar developmental

changes and finally contraction, which latter morbid process reacts on the ganglion cells, producing further degenerative changes in these bodies. The early stage of the active, hyperplastic, process of the connective tissue of the ganglia, attended, as we have shown it to be, by increased vascularity, produces an irritative condition of the ganglionic cells which reinforces the original active cause of the disease.

We cannot bring this paper to a conclusion without referring to two points which have an almost self-evident bearing on the affection we have shown to exist in the sympathetic ganglia; one is the condition of the minute vessels, both in the kidneys and elsewhere, which has attracted the attention of so many observers; the other, the yet more commonly known hypertrophy of the heart that is found in connection with Bright's disease.

With reference to the condition of all the smaller arteries of the kidney, when this organ is contracted, when, therefore, it has suffered from interstitial nephritis, all authors are agreed that thickening of the walls is present. Some observers, as Gull and Sutton, state that the thickening is due to a "hyalin-fibroid substance," deposited "chiefly outside the muscular layer." George Johnson, on the other hand, had previously affirmed that the thickening is due to a true hypertrophy of the muscular coat of the vessels. These authors have shown that a similar change affects the arteries of other organs of the body. Many observers have confirmed the existence of thickening of the arteries of the kidney, and have ranged themselves on one or the other side in reference to the nature of this change. Gull and Sutton differ materially from George Johnson in relation to the extent or parts of the vascular system involved in the change; their theory they have named "arterio-capillary fibrosis," implying by the name that the capillary vessels show the hyalin-fibroid changes as well as the small arteries, while Johnson's view necessarily limits the change to the arteries, which alone have muscular fibres in their wall.

From our own observations we have no hesitation in concluding, as is shown in the description of our specimens of this series of cases, as well as from the examination of very numerous other cases by comparison with healthy arterioles, that in cases of contracting kidney, the muscular tunics of the vessels are hypertrophied, especially and invariably in the kidney, and also in other organs of the body, even when the process of contraction is not far advanced. But we do not wish to enter into the discussion of this question, contenting ourselves with the statement just given of our belief concerning the true condition of the arterial changes—an opinion formed long previously to the investigations with which we are at present concerned. We wish, however, to point out the causal relations which we believe the muscular hypertrophy of the vessels has to the alterations found in the ganglia.

We do not think it rational to suppose that the muscular fibres contract,

for the purpose of lessening the supply of blood to the damaged kidneys, or for any other reason, from any power inherent in themselves. Such a notion implies a degree of intelligence or self-originating action which has never been attributed to muscular fibres, either of the voluntary or involuntary set; and, it seems to us, it is illogical to confer upon the muscular coats of the arterioles a power of self-action, which, in case of contracted kidneys, is sufficient to determine a substantial hypertrophy. The cause of this hypertrophy must be sought, since such action of the muscular fibres is not a voluntary one, in the ganglionic centres. Evidently the causal conditions must be general ones, because not only are the effects seen in both kidneys, but in many instances the vessels of other parts of the body are influenced; they must be causes that act on not only the renal plexus in particular, but also on the other ganglionic centres. One cause may be of such a nature that it operates through the general nervous system, for it is a well-ascertained fact that grief, and sorrow, and nervous depression are potent sources of Bright's disease, especially of the contracting kidney. Again, the disturbance may come through the blood; for the nutrient fluid supplying the renal plexus, if altered, will produce a condition of irritation of the ganglionic cells, with subsequent tissue-changes alike in the ganglia and in the kidneys, and give rise to the phenomena of interstitial nephritis—hyperplasia of the connective tissue, and hypertrophy of the vessels. We regard, then, both the tissue-changes and the hypertrophy as essential and connected parts of the same picture. Both conditions are presided over, and directed by, the sympathetic or vaso-motor centres.

Let us consider, in the next place, the hypertrophy of the left ventricle of the heart in its relation to these vascular changes, and also the place which this hypertrophy holds with reference to our theory. Hypertrophy of the heart, coexistent with chronic renal disease, was first alluded to by Bright in the first volume of *Guy's Hospital Reports*, and he expressed the opinion that the ventricular hypertrophy was due either to the direct action of the altered blood on the heart muscle or to the effect of this fluid on the minute and capillary circulation, so as to render greater action on the part of the heart necessary to force the blood through the distant subdivisions of the vascular system. Since Bright's time most pathologists have consented to this view of the causation of the cardiac hypertrophy, and have agreed that it was present in the majority of cases. But from the time that an essentially different pathological condition has been shown to exist in contracted kidneys and in the large white kidney, it has been pointed out that in the latter form of chronic Bright's disease the ventricular hypertrophy is exceptional.

Johnson was the first to offer a consistent theory for the cardiac hypertrophy with contracted kidney, founded on a physiological basis derived from a minute study of the anatomical parts. Gull and Sutton, while

denying the vascular hypertrophy, and thereby removing the antagonizing element which, according to Johnson's theory, is the cause of the cardiac hypertrophy, state that they "have particulars of nine cases in which the kidneys were very contracted and the heart was free from hypertrophy." Unfortunately, they do not refer us to the particulars of these cases. Johnson states that he has "observed a constant relation between hypertrophy of the arterial walls and hypertrophy of the left ventricle of the heart;" he also says that in the "majority of cases of contracted kidney the left ventricle is thickened," implying, therefore, that the cardiac hypertrophy is not invariable. In the waxy kidney, too, Grainger Stewart has shown that hypertrophy of the heart was present in only a small percentage of the cases.

We do not think that the heart hypertrophies simply, as has been assumed, because of the opposition the passage of blood meets with in the renal circulation. We are inclined to believe that the hypertrophy of both the heart and the vessels is to be traced to a central origin; in one case to the cardiac ganglia, and in the other to the renal. The same statement applies to the changes in the vessels and tissue in other organs of the body, and when they, in their turn, are affected, the ganglia which preside over them as centres most probably have been acted on in a similar manner as the ganglia already mentioned.

If cardiac hypertrophy invariably resulted from arterio-capillary narrowing, the change would certainly be vastly more common than it is. If simple narrowing were the cause, surely in the large white kidney the pressure on the capillary circulation is greater than in the early stages of contracted kidney, and therefore cardiac hypertrophy should be a marked feature of this form of chronic Bright's disease. Experience shows that it is not. In respect to the kidney itself, the secreting gland structure is just as much damaged, nay more so, in the large white kidney as it is in early stages of the granular kidney in which the vascular hypertrophy has occurred. There is, therefore, a deeper, a more remote origin of the vascular and of the cardiac hypertrophy; and we cannot but conclude that an essential difference in the pathology of the two forms of chronic renal disease exists in respect to their origin and, therefore, in respect to the cardio-vascular changes.

Further, it has been shown by Bamberger, that the cardiac hypertrophy occurs to a marked degree even in the early stages of contracting kidney or interstitial nephritis, before the kidney is much damaged; and this is, therefore, at a period of the disease when some other cause must be acting than the alterations of this organ or of its vessels.

That there should exist one case of hypertrophy of the vascular muscles in chronic Bright's disease with no cardiac hypertrophy, seems to destroy entirely the theory which Johnson has advanced; whereas, according to our belief of the central nervous origin of these hypertrophies, the occur-

rence of the two forms of hypertrophy is readily disconnected. The observations of Lubimoff furnish us with a direct anatomical basis on which to support this view. He relates many cases in which he examined all the principal ganglia, the cervical, the thoracic, and the solar, and found that the condition of the ganglion cells, the fibres, and the connective tissue differed in each centre respectively, even in patients dying of some general disease. One instance will serve for an illustration of this point; in a body of a patient who died of carcinoma of the pelvic viscera, with an extension of the malady to the general peritoneal surface, some of the ganglia of the solar plexus were diseased, not by an involvement in the new growth, while the superior ganglia showed nearly normal conditions. Similarly, we hold that the renal ganglia may be affected while the cardiac ganglia escape. That both are affected we believe to be the rule in cases of contracted kidney.

But we will not speculate any further in this matter. We had hoped to have furnished convincing reports of the state of the cardiac ganglia and their relation to hypertrophy of the heart. But our preparations thus far have not been fortunate, and we shall merely express our opinion that the cardiac ganglia exhibit changes similar to those described in the renal ganglia. Several other inquiries suggested themselves which we had desired to complete, such as an explanation from the point of view brought forward of the many nervous phenomena of Bright's disease, and of the state of the spinal cord at the origin of the filaments communicating with the ganglia. Yet we felt that we had arrived at results sufficiently distinct not to delay any longer the publication of what we had gained, and to invite others into the field for the benefit of the common cause.

In summing up our work, we think we have arrived at these conclusions:—

1st. That in Bright's disease, especially in the contracting kidney, there exists a constant lesion of the renal plexus.

2d. That whilst this lesion might be looked upon as forming part of a general process of degeneration, in connection with the kidney disease, we think it is the cause of the renal malady and precedes the degenerative changes.

3d. That the diseased condition of the ganglia furnishes the clue to the alterations of the vessels of the kidneys.

4th. That similar changes producing similar results may exist in other ganglia; for instance, in the cardiac plexus, explaining the hypertrophy of the heart.